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Subacute combined degeneration of the spinal cord in a vegan

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SUBACUTE combined degeneration of the spinal cord in nutritional vitamin B₁₂ deficiency states, though a rare complication, has been reported several times (Badenoch, 1954; Wokes, 1956; Smith, 1962; Connor & Pirola, 1963; Riley, 1966; Verjaal & Timmermans, 1967), and its association with veganism (vegans are people who exclude all forms of animal products from their diet) has been duly stressed by Wokes (1956) and Smith (1962). Although vegans would appear to be highly vulnerable subjects for deficiency disease, in fact the incidence of manifest symptoms and signs due to vitamin B₁₂ deficiency is rare, even when the serum levels are well below the range found in pernicious anaemia (Smith, 1962). The reason for this anomaly is not clear, though Smith (1962) advanced the view that tobacco smoking in vitamin B₁₂ deficiency states plays a definite role in the genesis of neurological complications, and of his reported cases, the only two patients with subacute combined degeneration of the spinal cord were smokers.

We consider our patient unique in the sense that she was a vegan who was a non-smoker but nevertheless she developed subacute combined degeneration of the spinal cord.

Case report

Miss D. A., aged 62 years, was admitted to Wythenshawe Hospital on 6.10.69 under the care of Dr C. D. R. Pengelly for the investigation of unsteadiness of gait and stiffness of her lower limbs. Her symptoms had started gradually over a 3-year period with tingling of hands and feet. She had noticed that handling money was difficult because it felt like sandpaper. Subsequently her gait became progressively ataxic until she was house-bound. Eventually she had to hold on to furniture to remain upright. Ten days before admission she fell and sustained a left Colles' fracture. She dismissed this

as a bruised wrist and sought no medical treatment. The consequent lack of mobility and pressure from her neighbours led to her admission to hospital.

There was no significant history of past illness. She had been a vegetarian since 1943 and for 5 years prior to admission she had been a vegan. She had been a non-smoker and teetotaler all her life.

On admission physical examination revealed no evidence of malnutrition and there was no pallor. Examination of the alimentary, cardiovascular and respiratory systems revealed no abnormality. BP 170/90 mmHg, routine urine examination normal. Examination of the nervous system was as follows: mentality normal; cranial nerves normal; there was no abnormality in the power, tone or reflexes in the arms; the lower limbs were slightly spastic, she could hardly stand on her feet and she was completely unable to walk without support; Romberg's sign was strongly positive; both ankle jerks were diminished; plantar responses on both sides were extensor; there was slight diminution of light-touch and pin-prick sensation over feet and hands; vibration sense was completely absent up to the lower end of the sternum and joint sensation was grossly impaired in both lower limbs.

Investigations. Hb 10.5 g/100 ml, PCV 34%, MCHC 30%, WCC 5000/mm³. Peripheral blood film: some macrocytes, normal differential count. RBC normochromic. Blood urea 35 mg/100 ml, mid-stream urine examination negative. Liver function tests normal. Serum protein levels: total 6.5, albumin 3.2, globulin 3.3 g/100 ml. Serum vitamin B₁₂ levels on two separate occasions were 71 and 72 pg/ml respectively. Serum folate 16 ng/ml. A bone marrow smear revealed megaloblastic erythropoiesis. A test meal showed the presence of free acid in the gastric juice. Faecal fat estimation on three successive occasions revealed normal values: 2.7, 1.5 and 3.5

g/24 hr. Barium meal examination including follow-through normal. Schilling test normal. (Urinary excretion of ^{57}Co -labelled vitamin B_{12} 12% in 24 hr) CSF: normal pressure, no increase in cells, protein 40 mg/100 ml, no increase in globulin. WR negative. X-ray of chest normal. X-ray of cervical spine: a mild degree of degenerative arthritic changes, C5-6. Sternal marrow following vitamin B_{12} therapy normal.

Treatment and course. She was treated with parenteral hydroxocobalamin because of her advanced neurological disease, 1000 μg initially for 1 week, subsequently changed to 500 μg , twice a week and then once very 6 weeks. This we had to do because she was not sure whether she would revert to a normal diet. Her neurological disabilities improved considerably with this treatment. Within 3 weeks she was able to stand and walk with help, her plantar responses became flexor and her bone marrow and blood films became normal. Vibration sense however did not improve.

Discussion

Our patient was a vegan of 5 years' duration. She had clinical features of subacute combined degeneration of the spinal cord, there were some macrocytes in the blood film and a megaloblastic bone marrow. The presence of free acid in the gastric juice, the normal Schilling test and the absence of any evidence of malabsorption excluded both pernicious anaemia and idiopathic steatorrhoea. Bourne & Oleesky (1960) suggested that to prove dietary vitamin B_{12} deficiency as a cause of macrocytic anaemia it is necessary to have the following criteria: (1) a megaloblastic bone marrow, (2) normal vitamin B_{12} absorption by one of the techniques using radio-active cyanocobalamin, (3) normal fat absorption, (4) the absence of complicating factors such as the taking of anticonvulsant drugs, pregnancy, or gastric operation, (5) a low serum level of vitamin B_{12} , (6) preferably the presence of free acid in the gastric juice, (7) conversion of the megaloblastic marrow to normoblastic by small oral doses of vitamin B_{12} . Our case fulfils all of these criteria, though the vitamin B_{12} was not administered orally because of her advanced neurological disease.

There is no clear explanation why manifest neurological complications are rarer than haematological changes in such a deficiency state, though EEG abnormalities have often been noted in nutritional vitamin B_{12} deficiency states (Walton *et al.*, 1954, West & Ellis, 1966). Unfortunately we could not arrange an early EEG in our patient. Smith (1962) in his study of veganism pointed out that hydroxocobalamin is the most active analogue of vitamin B_{12} . Cyanide in tobacco smoke is readily taken up by

hydroxocobalamin to form cyanocobalamin, and cyanide has been incriminated as a toxic factor in producing nerve damage. The haematological deficit can be corrected by small doses of the cobalamin portion of the vitamin B_{12} molecule, whereas hydroxocobalamin is necessary to protect against neurological complications. Both the cases reported by Smith (1962) were smokers and the serum vitamin B_{12} levels of the patients were 176 and 142 pg/ml, levels which were considerably higher than those found in our patient (71 and 72 pg/ml). Nevertheless, low levels of serum vitamin B_{12} are not necessarily associated with symptoms and signs. Mehta, Rege & Satoskar (1964) noted in a survey of healthy vegetarian medical students in India that more than half had a serum vitamin B_{12} level of less than 100 pg/ml without any symptoms and signs. This was again reported by Chanarin (1970). Smith (1962) believes that vegans, who are usually non-smokers and teetotallers, are protected from developing neurological complications because whatever limited quantity of vitamin B_{12} they possess is in hydroxocobalamin form.

We do not know for how long the very low serum level of vitamin B_{12} had been present in our patient, and it may be that the chronic low level was one factor in the aetiology of her neurological disease. The high levels of folic acid normally found in vegan diets may also have contributed to the development of the neurological picture. But the role of chronicity in low serum levels of vitamin B_{12} , and that of the high levels of folate in the vegan diet in the genesis of neurological disease are not clear.

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Multiple unusual abnormalities in the electrocardiogram in myxoedema

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DESCRIPTIONS of the electrocardiographic abnormalities in myxoedema have usually been confined to those of a sinus bradycardia, low-voltage QRS complexes, and T wave changes. Indeed, Wood (1968) described this combination as 'pathognomonic'. Additional changes, however, have been reported by other authors, including a prolonged Q-T interval (Hansen (1961), who also mentioned first degree heart-block), right bundle-branch block (Korth & Schmidt, 1955), complete heart-block (Ibrahim, 1957) and supraventricular and ventricular paroxysmal tachycardia. A sinus tachycardia, slowing after specific treatment, and unexplained on any other grounds than myxoedema, does not appear to have been cited previously; while inverted U waves also have not been described before in this disease.

Case report

A married woman of 53 was seen at out-patients with a 3-month history of fatigue, hoarseness, swollen hands, dry skin, puffy face, cramp in the feet, constipation, gain of a stone in weight, and recent cold intolerance. She had six children and had then been sterilized, but otherwise had an uneventful past history. Her menarche was at the age of 14½ and there was normal menstruation until the menopause at the age of 51. Particular questions were asked about possible anginal symptoms or other cardiac features, and none were elicited. There was no family history of any form of thyroid disease, diabetes mellitus, or pernicious anaemia, and no drugs had been taken in the remote or immediate past.

On examination her weight was 63 kg, height 1.5 m, temperature 35.5° C, pulse-rate 88, and blood-

pressure 130/80 mmHg. She appeared normally alert, but had slightly puffy eyelids, a rough and dry skin over her arms, and there was no palpable thyroid tissue. The relaxation phase of her ankle-jerks was clearly prolonged. The clinical diagnostic index score was + 41 (Billewicz *et al.*, 1969).

Investigations included: serum electrolytes: Na 138, K 4.0, Cl 101, total CO₂ 25 mEq/l; plasma calcium 10.6, 10.6 and 10.5 mg/100 ml; blood urea 45 mg/100 ml; protein-bound iodine (PBI) 1.4 and 1.6 µg/100 ml; serum cholesterol 428 mg/100 ml; Hb 14.2 g/100 ml; leucocytes 6,700/mm³ with normal differential count; urinalysis n.a.d.; negative autprecipitin test for thyroid autoantibodies. X-ray of chest showed no pulmonary or cardiac abnormality.

The electrocardiogram (Fig. 1) showed a sinus tachycardia (rate 120 in lead I), left axis, semi-horizontal position, normal voltage, widespread broadly-inverted U waves, and a prolonged Q-T interval (0.36 sec, the average for the rate being 0.28 sec corrected).

After 6 weeks treatment with thyroxine the electrocardiogram (Fig. 2) showed reduction of the sinus tachycardia to a rate of 100, a more horizontal position, increased voltage of all complexes generally, absence of U waves, and a normal Q-T interval. Normality of the ankle-jerks reflected a general clinical improvement in all respects, at the time of the repeat electrocardiogram.

Discussion

The clinical diagnosis of myxoedema appears certain in this case, but the pre-treatment electrocardiogram would suggest that this diagnosis was